

## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference IB/G-33580A/LEK	<b>FOR FURTHER ACTION</b> See Form PCT/PEA/416	
International application No. PCT/SI2004/000045	International filing date (day/month/year) 27.12.2004	Priority date (day/month/year) 29.12.2003
International Patent Classification (IPC) or national classification and IPC C07D405/06, C07D207/34		
Applicant LEK PHARMACEUTICALS D.D. et al.		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand  19.10.2005	Date of completion of this report  09.12.2005	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Fanni, S  Telephone No. +49 89 2399-8712	



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/SI2004/000045

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-10 as originally filed

**Claims, Numbers**

1-24 as originally filed

**Drawings, Sheets**

1/2-2/2 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/SI2004/000045

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1,16,22
Inventive step (IS)	Yes: Claims	
	No: Claims	1,16,22
Industrial applicability (IA)	Yes: Claims	1,16,22
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

Re Item V.

1 Reference is made to the following documents:

- D1 : WO 03/024959 A (EGIS GYOGYSZERGYAR RT; BARKOCZY, JOZSEF; SIMIG, GYULA; GREFF, ZOLTAN;) 27 March 2003 (2003-03-27)
- D2 : BAUMANN K L ET AL: "THE CONVERGENT SYNTHESIS OF CI-981, AN OPTICALLY ACTIVE, HIGHLY POTENT, TISSUE SELECTIVE INHIBITOR OF HMG-COA REDUCTASE" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 33, no. 17, 21 April 1992 (1992-04-21), pages 2283-2284, XP000608147 ISSN: 0040-4039
- D3 : EP 0 330 172 A (WARNER-LAMBERT COMPANY) 30 August 1989 (1989-08-30)
- D4 : US 5 155 251 A (BUTLER ET AL) 13 October 1992 (1992-10-13)
- D5 : WO 03/082816 A (RICHTER GEDEON VEGYESZETI GYAR RT; FISCHER, JANOS; VUKICS, KRISZTINA;) 9 October 2003 (2003-10-09)
- D6 : WO 02/43667 A (TEVA PHARMACEUTICAL INDUSTRIES LTD; TEVA PHARMACEUTICAL USA, INC; LIDO) 6 June 2002 (2002-06-06)
- D7 : WO 03/016317 A (TEVA PHARMACEUTICAL INDUSTRIES LTD; TEVA PHARMACEUTICALS USA, INC; NID) 27 February 2003 (2003-02-27)
- D8 : US 2003/109569 A1 (SORSAK GORAZD) 12 June 2003 (2003-06-12)

The present subject matter is directed towards amorphous form of present compound of formula I (claim 16), methods for the preparation of said compounds (claim 1) and its use in the synthesis of Atorvastatin.

Amorphous form of the present compounds are known from D1-D8, and the preparation of the same is disclosed in D2, D3 and D4. It appears therefore that both novelty (Article 33(2) PCT) and inventive step (Article 33(3)PCT) can be acknowledged for the present subject matter can be established only in a comparative manner, i.e. showing by the comparison of physical data that the amorphous form of compound of formula I disclosed in the present application clearly differs from those disclosed in the prior art and proving that the present polymorphic form can be regarded as the unexpected solution to a problem not yet solved by the prior art compounds. This does not appear to be the case with the present application. Thus, neither novelty nor inventive step can be acknowledged for the

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/SI2004/000045

present subject matter.